REMARKS

In order to expedite prosecution, claim 1 has been amended to focus on cyclic nucleotide analogs. The amendment adds no new matter.

Claims 2, 4-7, and 18-24 have been cancelled in view of the amendment to claim 1. The claims are cancelled without prejudice to prosecution in related applications. Claims 1, 3, 8-17, and 25-27 are currently pending. Claims 15-17 are withdrawn as drawn to a nonelected invention. Accordingly, claims 1, 3, 8-14, and 25-27 are under examination.

For convenience, the rejections will be addressed in the order set forth in the Office Action dated June 17, 2005.

Obviousness type double patenting rejection

Claims 1-3 and 8-12, and 25-27 were rejected for alleged obviousness-type double patenting over claims 1, 2, 7-13, 17-19, 22, 23, 28-34, 38-40, 44-46, 51-57, 61-67, and 72-78 of U.S. Patent No. 6,512,004; and over claims 1-4, 9-15, 26-28, 31-34, 39-45, and 56-59 of U.S. Patent No. 6,268,352. U.S. Patent Nos. 6, 512,004, U.S. Patent No. 6,268,352, and the subject application are commonly owned by The Regents of the University of California. Applicants will file appropriate terminal disclaimers upon identification of allowable claims.

Claims 1-3, 8-14, and 25-27 were also provisionally rejected for alleged obviousness-type double patenting over claims 1-3, 8-14, and 25-27 of co-pending Application No. 10/272,741. The cited applications and the subject application are commonly owned. Applicants will gladly consider filing an appropriate terminal disclaimers upon identification of allowable claims.

Rejection under 35 U.S.C. § 112, first paragraph, enablement

First, in order to expedite prosecution and in view of claims pending in related applications, the claims, including the generic claim, have been amended to focus on activators of protein kinase A and protein kinase G that are cAMP or cGMP analogs. Accordingly, the arguments focus on cyclic nucleotide analogs.

The Examiner acknowledges that the specification is enabled for all of the recited activators of cyclic nucleotide dependent protein kinases, including the exemplary cyclic nucleotide analogs (cAMP and cGMP analogs) listed in the specification and claims (*e.g.*, 8-bromo-adenosine 3',5'-monophosphate (8-Br-cAMP), 8-chloro-adenosine 3',5'-monophosphate (8-Cl-cAMP), 8-(4-chlorophenylthio)-cAMP, dibutyryl-cAMP, dioctanoyl-cAMP, Sp-cAMPS, Sp-8-bromo-cAMPS, 8-br-cGMP, 8-(4-chlorophenylthio)-cGMP, and dibutyryl-cGMP); but alleges that the specification does not reasonably provide enablement for the entire class of compounds that could act as activators of a cyclic nucleotide dependent protein kinase. Specifically, the Examiner argues that there are many protein kinases and that it would require undue experimentation to determine all of the affected protein kinases. It's further alleged that the specification fails to provide a nexus between screening and finding all compounds that act as potential activators and observing *in vivo* growth of damaged neurons post spinal injury following local administration of such compounds. In particular, the Examiner contends that Applicants have not provided structural features of activators, including cyclic nucleotide analogs, such that one of skill could reasonably expect to identify them. To the extent that the rejection is applies to the amended claims, Applicants respectfully traverse.

Cyclic nucleotide analogs and cyclic-nucleotide-dependent protein kinases are well known in the art

First, the claims are not directed to "any" protein kinase. The claims are directed to cyclic nucleotide dependent protein kinases. A simple search of the art makes it clear that this term has meaning to those in the art. Cyclic-nucleotide-dependent protein kinases, *i.e.*, cAMP and cGMP-dependent protein kinases, are well characterized enzymes and have been known in the art for many years. Included herewith in Appendix A is an exemplary publication from 1983 ("This Week's Citation Classic" cc/number 16, April 18, 1983), which demonstrate that even over fifteen years before the priority date of the instant application, the term "cyclic nucleotide dependent protein kinase" was well-established and common in the art. The Examiner has provided no evidence as to why one of skill in the art would not understand the use of this term.

Further, cyclic nucleotide analogs, such as cAMP and cGMP analogs, were also well known at the time of Applicants' invention. For example, the 1997 Sigma catalog, page 324, copy provided in Appendix B, shows various cyclic nucleotides listed under the heading "cyclic nucleotides", including cyclic nucleotide analogs exemplified in the specification, *e.g.,* 8-Br-cAMP. The term "cyclic nucleotide", and cAMP or cGMP analogs, must therefore logically have a readily recognizable meaning to those in the art in view of the this listing.

Undue experimentation is not required to identify cyclic nucleotide analogs useful in the invention

The Court of Appeals for the Federal Circuit has long recognized that in a rejection for undue experimentation that: "the key word is 'undue', not 'experimentation'". *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). This decision makes clear that a considerable amount of experimentation is permissible if it is merely routine, or if the specification provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. The MPEP reiterates this same conclusion (*see*, MPEP § 2164.06). In the present case, an assertion of undue experimentation must be supported by an explanation as to why the assays described in the specification for assessing neuron growth, *e.g.*, those set forth in the "Examples" section beginning on page 10, could not be used in a routine screen to confirm other cyclic nucleotide analogs as agents for use in the invention. Moreover, evidence or reasoning as to why such inhibitors would not be expected to have the same effect as 8-Br-cAMP, 8-Cl-cAMP, 8-(4-chlorophenylthio)-cAMP, dibutyryl-cAMP, dioctanoyl-cAMP, Sp-cAMPS, Sp-8-bromo-cAMPS, 8-br-cGMP, 8-(4-chlorophenylthio)-cGMP, or dibutyryl-cGMP on promoting neuron growth of neurons subject to growth inhibition by a neural cell repulsion factor must also be presented.

The current invention is the discovery that activators of cyclic nucleotide-dependent protein kinases promote neuron growth of neurons subject to growth inhibition by a neural cell repulsion factor. The invention is not cyclic nucleotide analogs. The law is clear.

You don't have to enable what is already known. *See, e.g., Application of Herschler*, 200 USPQ 711 (CCPA 1979).

In *Herschler*, the applicant had discovered that dimethylsulfoxide (DMSO) was useful as a transdermal carrier for physiologically active steroids. The CCPA found that a priority application describing a single steroid (dexamethasone 21-phosphate) supported a claim to the genus of all steroids. The CCPA explained that Herschler's claims were not drawn to a novel steroid but to the method of administration of steroids. As long as the class of steroids could be expected to be carried across the skin by DMSO, the claim could encompass any steroid, known or unknown. Following earlier case law, the CCPA reminded the Patent Office that the inventive principle was directed to a method of administration of steroids and that the specific steroid exemplified was not the point of patentability.

Herschler additionally provides guidance in identifying the inventive principle. There the court stated:

> The solicitor urges that the class of steroids is so large that a single example in the specification could not describe the varied members with their further varied properties. We disagree with this contention. Steroids, when considered as drugs, have a broad scope of physiological activity. On the other hand, steroids, when considered as a class of compounds carried through a layer of skin by DMSO, appear on this record to be chemically quite similar. (*Herschler* at 717)

Here, the facts are analogous. The instant invention concerns promoting neural cell growth using cyclic nucleotide analogs, not identification of new cyclic nucleotide analogs. There is no evidence that alternative cyclic nucleotide analogs would not be expected to work in the invention. Thus, the Examiner has failed to make a proper showing that the claims are not enabled. In view of the foregoing, Applicants respectfully request withdrawal of the rejection.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

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